

Natural products derived from plants as a source of drugs



Nature, the master of craftsman of molecules created almost an inexhaustible array of molecular entities. It stands as an infinite resource for drug development, novel chemotypes and pharmacophores, and scaffolds for amplification into efficacious drugs for a multitude of disease indications and other valuable bioactive agents. Since time immemorial, natural products have been the backbone of traditional system of healing throughout the globe, and have also been an integral part of history and culture. Although the use of bioactive natural products as herbal drug preparations dates back hundreds, even thousands, of years ago, their application as isolated and characterized compounds to modern drug discovery and development started only in the 19th century. It has been well documented that natural products played critical roles in modern drug development, especially for antibacterial and antitumor agents. Even though popularity of the synthetic products increased due to its production cost, time effectiveness, easy quality control, stringent regulation and quick effects, but their safety and efficacy was always remained questionable, resulting in the dependence on the natural products by more than 80% of the total population in the developing world, because of its time tested safety and efficacy. A huge number of natural product-derived compounds in various stages of clinical development highlighted the existing viability and significance of the use of natural products as sources of new drug candidates.

Until recently, plants were an important source of novel pharmacologically active compounds with many blockbuster drugs being derived directly or indirectly from plants. Despite the current preoccupation with synthetic chemistry as a vehicle to discover and manufacture drugs, the contribution of plants to disease treatment

and prevention is still enormous. Even at the dawn of 21st century, 11% of the 252 drugs considered as basic and essential by the WHO were exclusively of flowering plant origin.

Obviously natural products will continue to be extremely important as sources of medicinal agents. In addition to the natural products which have found direct medicinal application as drug entities, many others can serve as chemical models or templates for the design, synthesis, and semi synthesis of novel substances for treating humankind's diseases. Although there are some new approaches to drug discovery, such as combinatorial chemistry and computer-based molecular modeling design, and many drugs are made by synthetic chemistry, none of them can replaced the important role of natural products in drug discovery and development as most of the core structures or scaffolds for synthetic chemicals are based upon natural products.

According to Newman and Cragg 2012, the utility of natural products as sources of novel structures is still alive and well. Up to 50% the approved drugs during the last 30 years are from either directly or indirectly from natural products and in the area of cancer, over the time frame from around the 1940s to date, of the 175 small molecules 85 actually being either natural products or directly derived there from.

The use of plants as medicines has a long history in the treatment of various diseases. The plant-derived compounds have a long history of clinical use, better patient tolerance and acceptance. To date, 35,000-70,000 plant species have been screened for their medicinal use. Plants especially those with ethnopharmacological uses have been the primary sources of medicine for early drug discovery. Fabricant and Farnsworth, (2001) reported that, 80% of 122 plant derived drugs were related to their original ethnopharmacological purposes. Current drug discovery from plants mainly relied on bioactivity-guided fractionation and led to isolation of many important anticancer drugs such as paclitaxel, camptothecin etc.

The first commercial pure natural product introduced for therapeutic use is morphine marketed by Merck in 1826, and

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the first semi-synthetic pure drug aspirin, based on a natural product salicin isolated from *Salix alba*, was introduced by Bayer in 1899. This led to the isolation of early drugs such as cocaine, codeine, digitoxin, quinine and pilocarpine, of which some are still in use and several other recent plant derived compounds, which have undergone development and have been marketed as drugs which include Paclitaxel from *Taxus brevifolia* for lung, ovarian and breast cancer, Artemisinin from traditional Chinese plant *Artemisia annua* to combat multidrug resistant malaria, Silymarin extracted from the seeds of *Silybum marianum* for the treatment of liver diseases.

There is growing evidence that the old molecules are finding new applications through better understanding of molecular biology and clinical observations. For instance, the alkaloid, forskolin from *Coleus forskohlii* and phytochemicals from *Stephania glabra*, are now being rediscovered as adenylate cyclase and nitric oxide activators, which may help in preventing conditions including obesity and atherosclerosis.

During the last decade few plant derived drugs have been launched include Arteether, endoperoxide sesquiterpene lactone and semisynthetic natural product derived from Artemisinin used in malarial treatment, Nitisinone derived from natural product Leptospermone (*Callistemon citrinus*) is used in treatment of antityrosinaemia, galantamine is a natural alkaloid (obtained from *Galanthus nivalis*) for Alzheimer's, apomorphine is a semisynthetic compound derived from morphine (*Papaver somniferum*) used in

Parkinson's disease, Tiotropium a derivative of atropine from *Atropa belladonna* in chronic obstructive pulmonary disease, Dronabinol and Cannabidiol obtained from cannabis plant (*Cannabis sativa*) and Capsaicin active compound from *Capsicum annum* are used as pain relievers.

Natural products discovered so far have played a vital role in improving the human health and have been the drugs of choice despite facing a tough competition from compounds derived from computational and combinatorial chemistry, due to their safety and efficacy. The most striking feature of natural products in connection to their long lasting importance in drug discovery is their structural diversity that is still largely untapped.

Revitalization of the natural products is bringing newer challenges with respect to quality control and standardization along with cost effectiveness. The renewed interest in the development of natural products requires the confluence of the modern techniques and harmonization of regulations related to their research and development between various fields of science.

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